CERTIFICATION OF TRANSLATION

The undersigned, Brian John Fish, whose address is Apartment 602, 1530 16th Street, N.W., Washington, D.C. 20036 U.S.A., declares and states as follows:

I am well acquainted with the English and French languages; I have in the past translated numerous French documents of legal and/or technical content into English.

I have been requested to translate into English the French document identified as **French Patent Application No. 92 00062 for "Compositions for combating desquamation of the epidermis and scalp" filed July 1, 1992.**

To a copy of said French document I hereto attach an English translation and my Certification of Translation.

I hereby certify that the English translation of the above-cited French document identified as **French Patent Application No. 92 00062 for "Compositions for combating desquamation of the epidermis and scalp" filed July 1, 1992** is, to the best of my knowledge and ability, an accurate translation.

And I declare further that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, and that these statements and the like are punishable by fine and imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

April 22, 2002
Date

Brian John Fish
Brian John Fish

FR 2 685 867 – A1

(19) RÉPUBLIQUE FRANÇAISE

INSTITUT NATIONAL
DE LA PROPRIETÉ INDUSTRIELLE

PARIS

(11) Patent number: **2 685 867**
(only to be used when ordering copies)

(21) National registration N°: **92 00062**

(51) Int cl ⑤ : A61 K 7/06, 7/075

(12) **PATENT APPLICATION** **A1**

(22) Filed: July 01, 1992

(30) Priority:

(43) Date of Public Disclosure: July 09, 1993
Gazette 93/27

(56) References cited: see the end of this document

(60) References to other national documents:

(71) Applicant(s): THOREL Jean-Noël

(72) Inventor(s): THOREL Jean-Noël

(73) Owner(s)

(74) Agent: Cabinet Bruder

(54) Compositions for combating desquamation, of the epidermis and scalp

(57) Composition for combating desquamation and dandruff characterized in that the composition comprises the following physiologically acceptable components:

- at least one 1-hydroxy-2-pyridone, in pure or salt form possessing an alkyl radical having 1 to 4 C or phenyl radical at position 4, and an alkyl radical having 1 to 17 C, alkenyl radical having 2 to 17 C or cycloalkyl radical having 5 to 10 C at position 6,
- at least one undecylenic acid derivative,
- at least one optional preservative.

COMPOSITIONS FOR COMBATING DESQUAMATION OF THE EPIDERMIS AND SCALP

The present invention relates to novel compositions for combating desquamation of the epidermis and scalp which generally manifests itself in various forms such as exfoliation or dandruff, the said novel compositions being notably in the form of cream, mousse, shampoo or lotion.

The exfoliation problem of the epidermis, in the form of desquamation, and of the scalp, in the form of dandruff, is well known and many solutions have been proposed in the prior art, which have not been satisfactory due to their lack of effectiveness, high price, secondary effects, or even toxicity.

The ideal would be to achieve an optimum quality-to-price ratio and effectiveness-to-(toxicity + secondary effects) ratio. This is the applicant's intended objective in the present application.

Consequently, the functions of the compositions, according to the present invention, can be summarized as follows:

- Prevent bacterial proliferation and, in particular, that of Pityrosporum ovale;
- Decrease the thickness of the keratin layer and prevent desquamation and dandruff;
- Prevent pruritus.

These different points represent the main problems tied to desquamation and dandruff, and experience has shown that providing a solution would allow the principal causes and effects of exfoliation problems to be eliminated.

With the aim of providing such solutions, the objective of the present invention is to provide novel compositions in which the following physiologically acceptable components are associated:

- at least one 1-hydroxy, 2-pyridone, in pure or salt form, possessing an alkyl radical having 1 to 4 C or phenyl radical at position 4, and an alkyl radical having 1 to 17 C, alkenyl radical having 2 to 17 C, or cycloalkyl radical having 5 to 10 C at position 6;

according to a preferred embodiment of the invention, it can be in the form of an ethanolamine salt of hydroxy-1, methyl-4, (2,4,4-trimethyl pentyl)-6 (1H)-2-pyridone;

- at least one undecylenic acid derivative, and particularly one of the esters thereof with a sugar such as glycerol or sorbitol, or the products resulting from acylation by this acid, of amine acids such as those derived from the total acid hydrolysis of collagen;

- preferably, at least one preservative, such as phenoxyethanol.

As we will see later on, it turns out that associations according to the present invention and, in particular, the association of the two product families cited above, involve an unpredictable synergistic effect when the resulting effects are compared to those of the components taken separately.

The complementary use of the preservative further augments these effects and at the same time, of course, keeps them stable longer.

For a better understanding of the technical characteristics and the advantages of the present invention, we will describe examples of implementation, with the understanding, of course, that these are not limiting as regards their method of implementation and possible applications.

EXAMPLE 1: ANTI-PITYROSPORUM OVALE AND ANTI-SQUAMA CREAM

This cream can be applied as is or in the form of mousse on the epidermis and in particular on the skin and the scalp, notably in particularly acute cases of dandruff or seborrheic dermatitis secondarily infected by pityrosporum.

The cream is based on the following weight composition:

Phase A	concentrations	preference
Sorbitan undecylenate	0.3% to 2.0%	1.0%
Coconut oil	2.0% to 10.0%	5.0%
Triglycerides of saturated fatty acid and coco fractions (C8 to C10)	0.5% to 5.0%	1.0%

1-hydroxy, 4-methyl,		
(2, 4, 4-trimethyl pentyl)-6(1H)		
-2-pyridone ethanolamine salt	0.1 % to 0.4%	0.2%
C16 alcohol		0.5%
Dimethicone copolyol	0.3% to 2.0%	1.0%
Phase B		
Deionized water		86.2%
Polyacrylic	0.1 % to 0.5%	0.3%
Polyglycane	0.1% to 0.5%	0.3%
Phase C		
Deionized water		1.0%
99% triethanolamine	0.1% to 03%	0.2%
Phase D		
Phenoxyethanol	0.2% to 1.0%	0.3%
Phase E		
18-beta-glycyrrhetinic acid	0.1% to 2.0%	1.0%
Propylene glycol		2.0%

Phase E is made by mixing with agitation. Moreover, the polyacrylic is added to a third of the Phase B water heated to 75°C, then homogenized.

In the same way, the polyglycane is added to a third of the Phase B water heated to 75°C, then homogenized.

Finally, the two first thirds of water and contents thereof are progressively added to the last third of the Phase B water heated with moderate agitation to 75°C and the whole is emulsified.

Phase A is made with agitation at 75°C, sprinkling ethanolamine salt until total dissolution; then, this Phase A, under moderate agitation, is added to the emulsion obtained above, then Phase E is added. The whole is emulsified and left to cool to about 38°C while with moderate agitation.

Then, the components of Phase D are added, with high-speed homogenization, then Phase C is added, until homogenization for neutralization and is then left to cool to 30°C in order to get a sample for analysis and subsequent decanting.

Thus, a cream is obtained, which can be used as is, as said above, or in the form of mousse, which can be formed by any standard method, notably by using aerosol containers.

EXAMPLE 2: ANTI-DANDRUFF SHAMPOO

The shampoo is based on the following weight composition:

Phase A	concentrations	preference
Sodium laurylethersulfate		5.0%
Coco amidopropylbetaine		18.8%
Amine oxide		4.0%
Polymyristylglycolic ether of tallow fatty acids	0.5% to 3.0%	2.0%
1-hydroxy, 4-methyl, (2, 4, 4-trimethyl pentyl)-6(1H)-2-pyridone ethanolamine salt	0.5% to 1.5%	1.0%
Undecylenoyl-collagenic acid	0.2% to 2.0%	0.5%
Phase B		
Deionized water		61.7%
Willow vegetable oil-resin extract	0.05% to 0.2%	0.1%
Phase C		
Phenoxyethanol		0.4%
Phase D		
Ethoxyl sorbitan ester		0.1%

Phase E	
Crystallized citric acid powder	0.4%
Deionized water	5.0%
Dimethicone copolyol	1.0%

Phase B is prepared with moderate agitation at 50°C. Moreover, the amine oxide is melted with agitation at 80°C and the Talloweth 60 myristylglycol is sprinkled until dissolution, then cooled to about 70°C, before adding the other components of Phase A into Phase B, while maintaining it at 50°C. The whole is homogenized and left to cool to about 45°C, still with moderate agitation. Then the components of phases C, D and E are successively added. The homogenization is continued under moderate agitation, then slowly cooled to about 30°C. A sample is taken for control, and if the results are correct we proceed to decanting.

EXAMPLE 3: ANTI-DANDRUFF LOTION

The lotion is based on the following weight composition:

Phase A	concentrations	preference
Sorbitan undecylenate	0.5% to 1.5%	1.0%
Pyroctone olamine	0.1% to 0.8%	0.4%
Phase B		
Deionized water		84.95%
Polyacrylic		0.3%
Phase C		
Glycyrrhetinic 18 beta acid	0.2% to 2.0%	1.0%
Propylene-glycol		2.0%
Phase D		
Phenoxyethanol	0.1% to 0.5%	0.3%
Capric and caprylic acid		

glyceride	5.0% to 12.0%	10.0%
99% triethanolamine		0.05%

We proceed as follows:

Phase B is prepared by dispersing the polyacrylic under strong agitation in water; Phase C is prepared with moderate agitation; the components of Phase A are mixed by being heated progressively to 75°C and added into Phase B with agitation; Phase C is added, cooling to 40°C, and then the components of Phase D are added, continuing the cooling to 30°C.

It is to be noted that in the three examples above, we gave, on the one hand, the concentration ranges in the case of certain components, and, on the other hand, the preferred concentrations in accordance with the invention for all the components. Concerning the compositions of the three examples, the following experiments were performed, which illustrate well the remarkable properties of the invention products, especially when they are compared to product properties of the prior art.

IN-VITRO EXPERIMENTS

This involves making the comparisons that were just mentioned, i.e. those of the effects of said compositions in accordance with the invention, namely containing all active agents including 1-hydroxy, 2-pyridone salt with the effects of what we will call "bases", i.e. all components not considered as real active agents, but intended to form the physical support structure of the compositions, as well as with those same bases added to said salt.

The protocol followed is standard: we work with Petri dishes, preferably 90 mm; agar is seeded with suspensions of various germs; the excess suspension is aspirated; 13 mm diameter discs of sterile filter paper are soaked with the products on which experimentation is to occur, or these products are placed in wells punched out in agar and incubated at 37°C for 24 hours for the bacteria, or at room temperature for 48 hours for yeasts and fungi; we preferably work with four discs or wells per Petri dish; finally, the average width of the inhibition zones surrounding the discs and wells is measured. The results can be summarized as follows, the widths being in millimeters. For each example, the first column B gives the result for the base only, the second BS for the base and salt, and the third BSC for the base, the salt, and the composition according to the invention.

Microorganisms	EXAMPLE 1			EXAMPLE 2			EXAMPLE 3		
	B	BS	BSC	B	BS	BSC	B	BS	BSC
Pityrosporum ovale	2	5	9	5	2	24	0	6	16
Candida albicans	4	6	10	5	23	26	0	12	18
Aspergillus niger				4	22	24	0	8	15
Pseudomonas aeruginosa				8	17	18	0	5	9
Candida guillermodis				6	23	27			

The results are particularly significant because the addition of components according to the invention (BSC columns) presents inhibition zone widths superior to those obtained with the bases (B) and even with bases containing the salt (S), itself known in the prior art.

IN-VIVO EXPERIMENTS

Experiments were conducted for each composition of the three examples on eight male and four female individuals, all of them having at least one disorder of the type seborrhea, psoriasis, acne or alopecia in particular. The age range is from 18 to 65 years old with an average of 34 years old. We made a daily application over six weeks for cream, and twice per week for six weeks for shampoo and lotion, and the results were noted in the following manner:
Concerning dandruff, we take a sample of the squamae in a targeted zone of the vertex, and after smooth scraping with a spatula, applying a given section of glass tube with a rubber seal, in which we put a buffered serum containing a surfactant to put the squamae in suspension and dissociate cells; then cells are centrifuged and counted with a Burker cell microscope. These operations are performed on four fields of 16 squares; for that experiment, the subjects had a dandruff condition for seven years, on average.

For erythema and pruritus, an intensity from 0 to 3 was noted (0=nil, 1=light, 2=medium, 3=strong). Concerning the cream (example 1), it was applied in the following areas: nasogenien sulcus, eyebrows, and external auditory canal, with the chosen subjects having facial seborrheic dermatitis.

The following table gives the averages per group of 12 subjects, column 0 corresponding to the initial state, and columns 2, 4 and 6 to the respective states after 2, 4 and 6 weeks of treatment:

	EXAMPLE 1				EXAMPLE 2				EXAMPLE 3			
Week	0	2	4	6	0	2	4	6	0	2	4	6
Dandruff					26			10	25			12
Erythema	1.9	0.4	0.2	0	1.3	0.3	0	0	1.8	1.0	0.7	0
Pruritus	2.2	0.6	0.3	0.1	1.6	0.8	0.4	0.3	1.9	1.2	1.1	0.1

Here again, the results are convincing.

CLAIMS

1- Composition for combating desquamation and dandruff, characterized by the fact that the composition comprises the following physiologically acceptable components:

- at least one 1-hydroxy, 2-pyridone in pure or salt form, possessing an alkyl radical having 1 to 4 C or phenyl radical at position 4, and an alkyl radical having 1 to 17C, alkenyl radical having 2 to 17 C, or cycloalkyl radical having 5 to 10 C at position 6
- at least one undecylenic acid derivative.

2- Compositions according to claim 1, characterized by the fact that a 1-hydroxy-2-pyridone is in the form of the 1-hydroxy, 4-methyl, (2, 4, 4-trimethyl pentyl)-6(1H)-2-pyridone ethanolamine salt.

3- Composition according to one of claims 1 or 2, characterized by the fact that an undecylenic acid derivative is one of the esters thereof with a sugar such as glycerol or sorbitol.

4- Composition according to one of claims 1 to 3, characterized by the fact that an undecylenic acid derivative is a product resulting from the acylation, by this acid, of amine acids.

5- Compound according to claim 4, characterized by the fact that a product resulting from the acylation derives from total acid hydrolysis of collagen.

6- Composition according to one of claims 1 to 5, characterized by the fact that the composition includes at least one preservative.

7- Composition according to claim 6, characterized by the fact that one preservative is phenoxyethanol.

8- Cream characterized by the fact that it comprises one of the compositions according to one of claims 1 to 7.

9- Shampoo characterized by the fact that it comprises one of the compositions according to one of claims 1 to 7.

10- Lotion characterized by the fact that it comprises one of the compositions according to one of claims 1 to 7.

Translator/Reviewer's Note: The research report at the end of the French original (one page) has not been translated.